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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/554,941	05/22/2000	HOWARD JOHN ATKINSON	S-30287A	5118

22847 7590 04/10/2002
SYNGENTA BIOTECHNOLOGY, INC.
PATENT DEPARTMENT
3054 CORNWALLIS ROAD
P.O. BOX 12257
RESEARCH TRIANGLE PARK, NC 27709-2257

EXAMINER

KUBELIK, ANNE R

ART UNIT PAPER NUMBER

1638

DATE MAILED: 04/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/554,941

Applicant(s)

ATKINSON ET AL.

Examiner

Anne Kubelik

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) 15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-14, 16 and 17 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1, 3-13 and 16-17) in Paper No. 11, filed 15 January, 2002, is acknowledged. The traversal is on the ground(s) that no lack of unity was found in the international phase of this application and that it would not be a serious burden to examine all inventions. This is not found persuasive because examiners are not bound by the decision of other examiners, particularly foreign examiners, to examine all claims. Because the method of claim 1 is taught by the prior art, as detailed in the restriction requirement, the technical feature of an antipathogenic fusion protein is not special. Searching all groups would be an undue burden on the office, given the breadth of the claims. However, a search of the art uncovered art against Group II. As this Group has examination considerations similar to that of the elected Group, it will be examined as well.

Claim 15 is withdrawn from examination as being drawn to a non-elected invention.

Claims 1-14 and 16-17 are examined.

The requirement is still deemed proper and is therefore made FINAL.

2. The title of the invention is not descriptive of the claimed invention. The elected claims are directed to methods of improving pathogen resistance, DNA constructs used in the method and plants transformed with the constructs, while the present title is directed to fusion proteins. A new title is required that is clearly indicative of the invention to which the elected claims are directed. Note that titles can be up to 500 characters long.

3. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

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4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Within the specification there are sequences that are not accompanied by SEQ ID NOs: (e.g., pg 17, line 3).

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules and a response to the issues set forth below. Failure to fully comply with both of these requirements in the time period set for in this Office action will be held to be non-responsive.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claim 17 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, *i.e.*, results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

7. Claims 13-14 and 16 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 13-14 are drawn to DNA molecules encoding a fusion protein comprising two anti-pathogenic proteins joined by a linker peptide, which reads on any DNA molecule that encodes a protein with two anti-pathogenic domains. Claim 16 is

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drawn to any plant expressing such a DNA molecule, and thus reads on any plant that naturally encodes a protein with two anti-pathogenic domains. Thus, these are products of nature.

The DNA molecule and plants, as claimed, have the same characteristics and utility as those found in nature and therefore do not constitute patentable subject matter. See *American Wood v. Fiber Disintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). It is suggested that the claims be modified to refer to the hand of the inventor, e.g. by replacing "A" in claim 13 with --An isolated-- and indicating in claim 16 that the plant has been transformed with the DNA molecule. Alternatively, "molecule" in claim 13 (and the dependent claims) can be replaced with --construct--.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-14 and 16-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of DNA molecules that encode a fusion protein comprising any two anti-pathogenic proteins joined by a linker peptide of any size, methods of their use, and plants transformed with them. In contrast, the specification only

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describes coding sequences that encoding Oc-I, Oc-IAD86 and CpTI and linker peptides of SEQ ID NOs: 1, 2 and 11. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Hence, Applicant has not, in fact, described DNA molecules that encode a fusion protein comprising two anti-pathogenic proteins joined by a linker peptide within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997):

The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA Accordingly, the specification does not provide a written description of the invention

and at pg 1406:

a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, e.g., encoding human erythropoietin,

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because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

See *In re Shokal*, 113 USPQ 283, (CCPA 1957) at pg 285

It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. *In re Soll*, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; *In re Wahlforss et al.*, 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary. ...

We are of the opinion that a genus containing such a large number of species cannot properly be identified by the mere recitation or reduction to practice of four or five of them. As was pointed out by the examiner, four species might be held to support a genus, if such genus is disclosed in clear language; but where those species must be relied on not only to illustrate the genus but to define what it is, the situation is otherwise.

10. Claims 1-14 and 16-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of improving the nematode resistance of a plant by transformation with a DNA construct encoding the protease inhibitors Oc-IAD86 and CpTI joined by a linker peptide of SEQ ID NOs:1, 2 or 11, does not reasonably provide enablement for a method of improving the resistance of a plant to any pathogen by transformation with any DNA construct encoding any two anti-pathogenic proteins joined by a linker peptide of any size. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a method of improving the resistance of a plant to any pathogen by transformation with a DNA construct encoding two anti-pathogenic proteins joined by any linker peptide, DNA constructs used in the method and plants so transformed.

The instant specification, however, only provides guidance for DNA constructs encoding the protease inhibitors Oc-IAD86 and CpTI joined by linker peptides of SEQ ID NOs:1, 2 and 11

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(example 1), DNA constructs encoding the protease inhibitors Oc-I or CpTI (example 2), transformation of the constructs into plants (example 3) and *E. coli* (example 4), and purification of the proteins from *E. coli* and *Arabidopsis*, Western blots of proteins from nematodes feeding off of the transgenic plants and to proteins from the transgenic plants themselves, and production of antibodies to Oc-IΔD86 and CpTI (example 5).

The instant specification fails to provide guidance for use of DNA constructs encoding anti-pathogenic proteins of any size or linkers of any size. The specification fails to provide guidance for improving the resistance of a plant to any pathogen.

Not all proteins are small enough to be ingested by nematodes. Urwin et al (1997, Plant J. 12:455-461) teach that green fluorescent protein, which is approximately 28kDa, is too large to be ingested by *Heterodera schachtii* (pg 459, left column, paragraph 3). Thus, DNA constructs encoding fusion proteins that are too large will not be effective in the instant method.

Protease inhibitors, when expressed in a plant, do not provide resistance to all pathogens, including bacteria (Gleddie et al, 2000, "The control of plant pathogens with protease inhibitors: A realistic approach?", *In: Recombinant protease inhibitors in plants*, Michaud, ed., pg 53-64; see pg 59, left column, paragraph 1). Gleddie et al also teach that any protease inhibitor must be targeted to the appropriate cellular location and this location differs for different pathogens (pg 60, left column, paragraph 2). The instant specification fails to teach that Oc-IΔD86 and CpTI provide resistance to any pathogen other than nematodes and fails to teach the appropriate cellular targeting of the fusion protein.

In the absence of appropriate guidance, undue trial and error experimentation would be required to screen through the myriad of DNAs that encode proteins with antipathogenic activity,

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and plants transformed therewith, to identify those that confer increased pathogens resistance against the multitude of different pathogens as claimed.

Given the claim breath, unpredictability in the art, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1-14 and 16-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claims 1-12 are indefinite because they lack agreement between the preamble of the methods and the positive method steps. Methods must be circular; the final step must generate the item the method is intended to produce. For example, the method of improving pathogen resistance in a plant in claim 1 ends in integrating a gene into a plant, when it should end in the production a plant with improved pathogen resistance.

Claims 1 and 13 are indefinite because it is not clear if "with anti-pathogeneic activity" in parts (a) and (c) is intended to modify both protein" and "protein domain" or if it is intended to modify only "protein domain".

In claim 6 it is not clear if the promoter refers to the one that is part of gene, or if the promoter is in addition to the promoter that a part of the gene. Note, that "gene" refers to a DNA that comprises a promoter and an encoding region.

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Claim 12 makes no sense in its recitation of "The method according to claim 3 improving nematode resistance or tolerance". The claim would make sense if "improving nematode resistance or tolerance" were replaced with --, wherein nematode resistance or tolerance of the plant is improved--.

Claim 13 is indefinite in its recitation of "capable of". It is not clear that the DNA molecule actually does encode the fusion protein.

Claim 14 lacks antecedent basis for the limitation "the encoded fusion protein" in line 1.

Claim 17 provides for the use of a DNA molecule, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

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14. Claim 13 is rejected under 35 U.S.C. 102(b) as being anticipated by Warren et al (WO 96/10083).

Warren et al teach a maize-optimized DNA molecule (pCIB5531) encoding the anti-pathogenic proteins VIP2A(a) and VIP1A(a) linked by a linker peptide (pg 93).

15. Claims 1-3, 7, 12-14 and 16-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Anderson et al (WO 94/13810).

Anderson et al teach a nucleic acid encoding a type II serine protease inhibitor from *Nicotiana alata*, which contains 6 reactive domains; these domains are joined by linkers (Fig. 1 and pg 26-27). This protease inhibitor is proteolytically cleaved in plant tissues (pg 29 and 32-33) and inhibits casein hydrolysis by crude gut extracts of various insects (Table 3). Anderson et al also teach a method of using this nucleic acid to increase resistance of a plant to insect or other pathogen infestation and plants so transformed (claims 25-28).

16. Claims 1-3, 7, 12-14 and 16-17 are rejected under 35 U.S.C. 102(e) as being anticipated by Anderson et al (US Patent 6,031,087, 102(e) date September, 1995).

Anderson et al teach a nucleic acid encoding a type II serine protease inhibitor from *Nicotiana alata*, which contains 6 reactive domains; these domains are joined by linkers (Fig. 1 and column 17, lines 12-39). This protease inhibitor is proteolytically cleaved in plant tissues (pg column 18, line 56, to column 19, line 17; column 20, lines 1-43) and inhibits casein hydrolysis by crude gut extracts of various insects (Table 3). Anderson et al also teach a method of using this nucleic acid to increase resistance of a plant to insect or other pathogen infestation (claim 7).

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17. Claim 13 is rejected under 35 U.S.C. 102(b) as being anticipated by Atkinson et al (WO 96/16173).

Atkinson et al teach DNA constructs encoding the anti-pathogenic protease inhibitors chicken egg white cystatin linked to oryzacystatin joined by various linker peptides (pg 22-24). Some of the linker peptides would be cleaved by a plant and some would not. Atkinson et al also teach a nucleic acid encoding a modified version of oryzacystatin, Oc-IAD86 (paragraph spanning ph 17-18) and a method of using it to increase resistance of tomato roots to nematodes (pg 20-21). Atkinson et al also disclose plants transformed with the DNA fusion constructs and DNA fusion constructs encoding Oc-IAD86 and another protein (claims 47-48).

18. Claim 13 is rejected under 35 U.S.C. 102(b) as being anticipated by Mapelli et al (1992, EP 497,366).

Mapelli et al teach DNA constructs encoding multimers of anti-microbial proteins joined by a "bridge" or linker peptide (ph 5, line 51, to pg 6, line 11; example 22).

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

20. Claims 1-5, 7-8, 12-13 and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Atkinson et al (*supra*) in view of Lilley et al (1996, Parasitology 113:415-424).

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The claims are drawn to a method of improving pathogen resistance or tolerance in plants by transformation with a DNA molecule that encodes a fusion protein comprising two anti-pathogenic proteins or domains joined by a linker peptide, wherein one of the antipathogenic proteins is cowpea trypsin inhibitor (CpTI) or Oc-IAD86, DNA constructs used in that method and plants so transformed.

The teachings of Atkinson et al are discussed *supra*. Atkinson et al do not teach constructs in which CpTI is one of the protease inhibitors.

Lilley et al teach the genes for Oc-IAD86 and CpTI (pg 416, right column , paragraph 3) and the effectiveness of the proteins in inhibiting cyst-nematode proteases (pg 417-420).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of using DNA fusion constructs encoding anti-pathogenic protease inhibitors joined by various linker peptides to increase resistance of plant roots to nematodes as taught by Atkinson et al, to use the CpTI gene described in Lilley et al in the constructs. One of ordinary skill in the art would have been motivated to do so because Lilley et al state that the cleavage of certain protease substrates by nematode gut extracts can only be inhibited by a combination of both Oc-IAD86 and CpTI (pg 422, left column, paragraph 2) and suggests expressing both in a plant (pg 423, left column, paragraph 1).

21. Claims 1-8, 12-13 and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Atkinson et al in view of Hepher et al (1992, EP 502,730) and Conkling et al (US Patent 5,837,876, filed July, 1995).

The claims are drawn to a method of improving pathogen resistance or tolerance in plants by transformation with a DNA molecule that encodes a fusion protein comprising two anti-

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pathogenic proteins or domains joined by a linker peptide, wherein one of the antipathogenic proteins is cowpea trypsin inhibitor (CpTI) or Oc-IAD86, and wherein the constructs are expressed from root-specific promoters, DNA constructs used in that method and plants so transformed.

The teachings of Atkinson et al are discussed *supra*. Atkinson et al do not teach constructs in which CpTI is one of the protease inhibitors, nor do they teach expression of the constructs behind root-specific promoters.

Hepher et al teach a method of producing nematode resistant potato plants by transformation with a DNA construct encoding CpTI (example 1-2) and isolation of the gene for oryzastatin (example 6).

Conkling et al teach a root specific promoter from tobacco (SEQ ID NO:1).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of using DNA fusion constructs encoding anti-pathogenic protease inhibitors, including Oc-IAD86, joined by various linker peptides to increase resistance of plant roots to nematodes as taught by Atkinson et al, to use the CpTI gene in those constructs as described in Hepher et al and to use the root-specific promoter taught by Conkling et al. One of ordinary skill in the art would have been motivated to do so because of the suggestions of Hepher et al to express the constructs behind root-specific promoters (pg 5, lines 40-45) and of Conkling et al to use the promoter to express gene for resistance to below-ground organisms like nematode (column 5, lines 21-30, and column 6, lines 39-67). Use of the CpTi gene in the constructs of Atkinson et al would be an obvious refinement of experimental parameters.

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22. Claims 9-11 are free of the prior art, given the failure of the prior art to teach or suggest a method of improving pathogen resistance or tolerance in plants by transformation with a DNA molecule that encodes a fusion protein comprising two anti-pathogenic proteins or domains joined by a linker peptide of SEQ ID NOs: 1, 2 or 11.

Conclusion

23. No claim is allowed.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Kimberly Davis, at (703) 305-3015.

Anne R. Kubelik, Ph.D.
April 8, 2002



**AMY J. NELSON, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600**